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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,410	11/17/2005	Giovanni Paganelli	725.1049	4581
20311 7590 05/10/2010 LUCAS & MERCANTI, LLP 475 PARK AVENUE SOUTH 15TH FLOOR NEW YORK, NY 10016				
EXAMINER GUSNOW, ANNE				
ART UNIT		PAPER NUMBER		
1643				
NOTIFICATION DATE		DELIVERY MODE		
05/10/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary

Application No.

10/554,410

Applicant(s)

PAGANELLI ET AL.

Examiner

Anne M. Gussow

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-7,9,11-14 and 18-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-7,9,11-14 and 18-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB06)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. No claims have been amended, added, or cancelled with the response filed March 2, 2010.
2. Claims 1, 3-7, 9, 11-14, and 18-39 are under examination.

Rejections Maintained

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Applicant's arguments filed March 2, 2010 have been fully considered but they are not persuasive. The response states that Rusckowski only provides for a method for imaging osteomyelitis (an infection of the bones) with streptavidin and biotin (e.g., the abstract). Rusckowski also discloses that first, unlabelled streptavidin was administered and allowed to accumulate nonspecifically into the lesion, probably in a manner similar to polyclonal IgG, then, the radiolabel was delivered bound to biotin (e.g., page 1655, right col, lines 12-16). Further, Rusckowski discloses that biotin alone is also very successful in detecting infected lesions (e.g., page 1659, right col., first paragraph). Samuel also does not disclose Applicants' invention. Samuel describes a method to

detect infections (prosthetic vascular graft infection) by i.v. injection of unlabelled streptavidin followed by labeled biotin (e.g., page 55, left col, first paragraph and right col., second full paragraph). Samuel also, as Rusckowski above, discloses that unlabeled avidin is a protein which accumulates non-specifically at sites of inflammations (e.g., page 55, right col., second full paragraph). As such, neither Rusckowski nor Samuel discloses, teaches or even suggests the presently claimed method of treating a patient with solid tumor by first administering intraoperatively a first agent as avidin, streptavidin, etc and then administering postoperatively a second anticancer agent having affinity for the first. As previously submitted, Goldenberg only provides for a method for injecting a patient with a first composition comprising either streptavidin- or avidin-conjugated antibody, biotinylated antibody to be used in conjunction with avidin and biotin...wherein the antibody is an antibody or an antibody fragment which specifically binds a marker produced by or associated with the lesion (e.g., page 1, paragraph [0003], page 3 paragraph [0036]). As also previously submitted, the first composition of Applicants' invention does not contain a monoclonal antibody and the affinity for the tumor is provided by avidin only. Cokgor does not provide for the missing links in that it suffers from the same defects. Cokgor also discloses the administration of I- 131 labeled antibody administered into surgically created resection cavities in patients suffering from malignant gliomas (e.g., the abstract). As such, the combination of Rusckowski or Samuel with Goldenberg and Cokgor still is not the presently claimed invention. MacPhee also does not add anything to the combination of Rusckowski or Samuel with Goldenberg and Cokgor. MacPhee

only discloses a fibrin sealant dressing which could be supplemented with a number of drugs to prevent infections, inflammations etc (e.g., the abstract).

Response to Arguments

In response to these arguments, as set forth in the office action mailed December 8, 2009, neither Rusckowski nor Samuel teach treatment of cancer. However, both of these references speak to the use of an avidin/ biotin system for targeting specific tissues by using an unlabeled and nonspecific avidin. Both Goldenberg and Cokgor teach the use of an avidin/biotin system for the treatment of cancer. Goldenberg clearly contemplates the avidin/biotin components to be interchangeable in so far as which is administered first (paragraph 36), thus the fact that the avidin of Goldenberg is conjugated to an antibody is not relevant to the instant rejection. While one of ordinary skill in the art would recognize that an antibody which binds to a tumor marker would increase the concentration on the tumor cells, such an antibody would not be essential for the method since Goldenberg teaches the biotin which does not contain an antibody could be administered 24 hours before the avidin compound and since both Rusckowski and Samuel teach the use of an unlabeled and nonspecific avidin. Further, Cokgor teaches that systemic administration of antibodies are not as effective in the treatment of brain tumors because antibodies do not cross the blood brain barrier well, and the instant claims read on the treatment of a brain tumor. Regarding the sealant of MacPhee, MacPhee teaches a spray method of administering a pharmaceutical composition. MacPhee teaches that the sealant may be

supplemented with other factors including growth factors, drugs, or antibodies.

Therefore, one of ordinary skill in the art would recognize that spray administration is an acceptable method of delivering a pharmaceutical agent (in the instant case avidin) to a localized area (in the instant case on a tumor). Thus, one of ordinary skill in the art would be motivated to and had a reasonable expectation of success to have used the unlabeled agent of Rusckowski or Samuel in the method of treating cancer of Goldenberg or Cokgor with the spray administration of MacPhee.

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, as set forth above, when taken together one of ordinary skill in the art would recognize that the avidin/biotin system would be useful for targeting tumor cells by administration intraoperatively directly into a tumor cavity.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

Conclusion

5. No claims are allowed.
6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
May 3, 2010

/Anne M. Gussow/
Examiner, Art Unit 1643